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10/553,596	10/18/2005	Rena Nishizawa	Q90950	4644
65565	7590	12/28/2007	EXAMINER	
SUGHRUE-265550			MURRAY, JEFFREY H	
2100 PENNSYLVANIA AVE. NW			ART UNIT	PAPER NUMBER
WASHINGTON, DC 20037-3213			1624	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/553,596	<b>Applicant(s)</b> NISHIZAWA, RENA
	<b>Examiner</b> JEFFREY H. MURRAY	<b>Art Unit</b> 1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 04 October 2007.
- 2a) This action is FINAL.      2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1,4,7-10,19 and 21 is/are pending in the application.
- 4a) Of the above claim(s) 19 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1,4,7-10 and 21 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO/95/08)  
 Paper No(s)/Mail Date \_\_\_\_\_
- 4) Interview Summary (PTO-413)  
 Paper No(s)/Mail Date \_\_\_\_\_
- 5) Notice of Informal Patent Application
- 6) Other: \_\_\_\_\_

**DETAILED ACTION**

***Status of Claims***

1. Claims 1-7 and 9 are rejected. Claim 8 is allowed. Claims 10-19 are withdrawn.
2. Claims 1, 4, 7-10, and 21 are pending in this application. Claims 2, 3, 5, 6, 11-18 and 20 have been cancelled. This action is in response to the applicants' amendment after a non-final and reply filed on October 4, 2007.

***Status of Objections***

3. Claim 1 are objected to as being vague and indefinite. The objection to the specification is hereby withdrawn in view of applicants' amendments to the Claim.
4. Claim 4 are objected to as being vague and indefinite. The objection to the specification is hereby withdrawn in view of applicants' amendments to the Claim.

***Status of Rejections***

5. Claims 1-7 and 9 are rejected under 35 U.S.C. 102(b), as failing to comply with the novelty requirement. The rejection of Claims 1-7 and 9 are hereby moot and withdrawn in view of applicants' cancellation of Claims 2, 3, 5, 6, and applicants amendments to Claim 1 and 4.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

***New Rejections***  
***Claim Rejections - 35 USC § 112***

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 has been amended by the applicants. After amendment the Claim now reads, in pertinent part, "...provided that 9-benzyl-1,3-dimethyl-1,3,9-triazaspiro[5.5]undecan-2,one; 1,3-dimethyl- 1,3,9-triazaspiro[5.5]undecan-2-one; 9-benzyl- 1 -methyl-1,3,9,triазаспиро[5.5]-undecan-2-one; and 1-methyl-1,3,9,triазаспиро[5.5]undecan-2-one are excluded."

Unless this particular exclusion of compounds has been described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, it cannot be permitted within the claim. Negative provisos within a claim are not permitted unless the explicit negative proviso is described within the specification as well.

8. Claims 1, 4, 7-10 and 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds, a

Art Unit: 1624

salt thereof, or a quaternary ammonium salt thereof, the specification does not reasonably provide enablement for N-oxides thereof, solvates thereof, or prodrugs thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

9. The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation. (*United States v. Teletronics Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based on a single factor, but rather a conclusion reached by weighing many factors (See *Ex parte Forman* 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988)). These factors include the following:

1) *Amount of guidance provided by Applicant.* While the Applicant has demonstrated within the application how to make numerous compounds and compositions, only compounds or their salts have been demonstrated. No other compounds or compositions which are N-oxides, solvates, or prodrugs have been described or demonstrated.

2) *Unpredictability in the art.* It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. (USPQ 18, 24 (CCPA 1970). See *In re Fisher*, 427 F.2d 833, 839, 166.

Art Unit: 1624

The scope of N-oxide is not adequately enabled or defined. Applicants provide no guidance as how the compounds are made or where the N-oxide is located on the compound or composition. The current compounds and compositions all contain at least 3 nitrogens, including the two nitrogens in the piperidinone ring and the nitrogen in the piperidine ring which could conceivably be bonded to an N-oxide are considered.

The scope of "solvate" is not adequately enabled or defined. Applicants provide no guidance as how the compounds are made more active *in vivo*. Solvates cannot be predicted and therefore are not capable of being claimed if the applicant cannot properly enable a particular solvate.

"Predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult. Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compounds. Certain molecular shapes and features favor the formation of crystals without solvent; these compounds tend to be stabilized by efficient packing of molecules in the crystal lattice, whereas other crystal forms are more stable in the presence of water and/or solvents. There may be too many possibilities so that no computer programs are currently available for predicting the crystal structures of hydrates and solvates. (Vippagunta et. al. Advanced Drug Delivery Reviews 48 (2001) 3-26.

The scope of "prodrug" is not adequately enabled or defined. Applicants provide no guidance as how the compounds are made more active *in vivo*. The choice of a "prodrug" will vary from drug to drug. Therefore, more than minimal routine experimentation would be required to determine which prodrug will be suitable for the instant invention. The application does not provide any guidance

Art Unit: 1624

for one skilled in the art on how the prodrug is converted to active compounds, by what mechanisms and at what site the prodrug will be activated, what in vivo enzymes are likely involved in cleaving the protected group, etc.

3) *Number of working examples.* Applicant has provided no examples of any N-oxides, solvates or prodrugs of compounds or compositions of formula I.

4) *Scope of the claims.* The scope of the claims involve all of the compounds and compositions of general formula I, therefore the scope of the claims is very broad.

5) *Nature of the invention.* The nature of this invention relates generally to spiro-piperidine compounds having chemokine receptor antagonism which are useful as medicines, drugs comprising them as active ingredients, and production methods and uses thereof

6) *Level of skill in the art.* The artisan using Applicants invention would be a chemist with a M.S. or Ph.D. degree, and having several years of bench experience.

MPEP §2164.01 (a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here that Applicant is not enabled for making most of the compounds or compositions mentioned in the current application.

Art Unit: 1624

***Conclusion***

10. Claims 1, 4, 7-10, and 21 are rejected.
11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey H. Murray whose telephone number is (571) 272-9023. The examiner can normally be reached on Mon-Thurs. 7:30-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a US PTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey H Murray/  
Examiner, Art Unit 1624

/James O. Wilson/  
Supervisory Patent Examiner  
Art Unit 1624

